

REMARKS

Reexamination and reconsideration of the subject application, pursuant to and consistent with 37 C.F.R. § 1.113, are respectfully requested in light of the remarks which follow.

Status

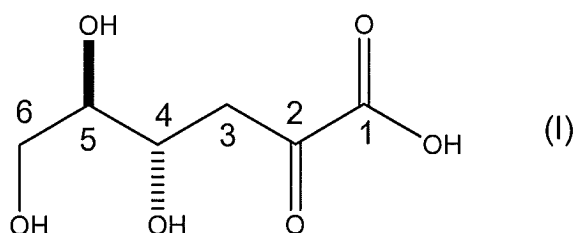
As is correctly reflected in the Office Action Summary, Claims 49-67 and 70-89 are pending. *Final Office Action mailed January 25, 2010, Office Action Summary, Item 4.* Claims 52-67 and 83-89 have been withdrawn from consideration. *Id. at Item 4a.* Claims 49-51 and 70-82 stand rejected. *Id. at Item 6.*

Acknowledgement has been made to Applicants' claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f), and certified copies of the priority documents have not yet been received from the International Bureau. *Id. at Item 12(c)(3).*

Summary of Amendments

By the foregoing amendments, Applicants amended independent Claim 49 to read:

A method for producing 2'-deoxynucleosides or 2'-deoxynucleoside precursors, wherein said 2'-deoxynucleoside precursors are 2-deoxy-D-ribose (DRI) or carbohydrate compounds which can be converted into the 2-deoxy-D-ribosyl moiety of 2'-deoxynucleosides, including 1-phospho-2-deoxy-D-ribose, 5-phospho-2-deoxy-D-ribose, 2-deoxy-D-ribitol, 2-deoxy-D-ribonic acid, 2-deoxy-D-ribono-1,4-lactone, 1-N-morpholino-3,4,5-trihydroxy-pentene-1, and their derivatives, from a compound of formula (I), or its salts,



or a protected form thereof wherein one or more of the hydroxyl groups at positions 4, 5, and/or 6 are protected by a protection group in a process comprising a decarboxylation step; wherein the decarboxylation step is effected by an enzymatic reaction comprising a single step, and the enzymatic reaction is catalyzed by an enzyme having keto acid decarboxylase activity.

Support for these amendments may be found throughout the Specification, and at least at Page 5, Lines 9-16 and at Page 5, Line 22 to Page 6, Line 4, of the Specification. Accordingly, no new matter has been added.

Priority

On Page 2 of the Final Office Action mailed January 25, 2010, Applicants' claim for foreign priority to European Patent Application No. 03013457.1, filed on June 24, 2003, and to European Patent Application No. 03027750.3, filed on December 2, 2003 (together, "the European Priority Applications"), is acknowledged by the Examiner. See *Final Office Action mailed January 25, 2010, Page 2*. The Examiner also reiterates that Applicants have not filed certified copies of the European Priority Applications. *Id.*

The instant application is a national stage application pursuant to 35 U.S.C. § 371 of International Patent Application No. PCT/EP2004/006848, filed on June 24, 2004, and published as WO 2004/113358 on December 29, 2004. PCT Rule 17.2(a)

requires *the Patent Office* to obtain certified copies of the priority documents from the International Bureau. Accordingly, Applicants respectfully request that *the Patent Office* obtain certified copies of the European Priority Applications and acknowledge receipt thereof in the next official communication to Applicants. For the Examiner's convenience, the text of PCT Rule 17.2(a) is listed below.¹

Rejections Under 35 U.S.C. § 112, First Paragraph – Written Description

Claims 49-51 and 70-82 were rejected under 35 U.S.C. § 112, First Paragraph, as purportedly lacking sufficient written description due to the phrase “a protected form thereof” in Claims 49-51. *See Office Action mailed January 25, 2010, Pages 3-8.*

These rejections are respectfully traversed.

The fundamental factual inquiry for written description is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the

¹ 17.2 *Availability of Copies* (a) Where the applicant has complied with Rule 17.1(a), (b) or (b-bis) the International Bureau shall, at the specific request of the designated Office, promptly but not prior to the international publication of the international application, furnish a copy of the priority document to that Office. ***No such Office shall ask the applicant himself to furnish it with a copy.*** The applicant shall not be required to furnish a translation to the designated Office before the expiration of the applicable time limit under Article 22. Where the applicant makes an express request to the designated Office under Article 23(2) prior to the international publication of the international application, the International Bureau shall, at the specific request of the designated Office, furnish a copy of the priority document to that Office promptly after receiving it. (b) The International Bureau shall not make copies of the priority document available to the public prior to the international publication of the international application. (c) Where the international application has been published under Article 21, the International Bureau shall furnish a copy of the priority document to any person upon request and subject to reimbursement of the cost unless, prior to that publication: (i) the international application was withdrawn, (ii) the relevant priority claim was withdrawn or considered, under Rule 26bis.2(b), not to have been made. (emphases added).

filing date sought, the Applicants were in possession of the invention now claimed. See, e.g., *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 U.S.P.Q.2d 1111, 1117 (Fed. Cir. 1991). Applicants submit that the instant application conveys with reasonable clarity to those skilled in the art that Applicants were in possession of the subject matter of Claims 49-51 and 70-82.

The specification clearly defines compounds of formula (I) or its salts “or a protected form thereof” as compounds or their salts wherein one or more of the hydroxyl groups at positions 4, 5, and 6 are replaced by protecting groups. *Specification, Page 5, Lines 22-25*. Suitable protection groups were well-known and had been extensively studied as of the filing date of the present application. Moreover, a representative number of suitable protection groups are explicitly set forth in the specification. See, e.g., *Specification, Page 5, Line 22 to Page 6, Line 4*. Based on at least the foregoing, not only would one of ordinary skill in the art understand what is meant by a compound of formula (I) or its salts “or a protected form thereof,” he would understand that Applicants were in possession of the subject matter of Claims 49-51 and 70-82 at the time of filing.

It is important to recognize that “[c]laim terms should generally be given their ordinary and customary meaning and . . . such meaning is one ‘that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application.’ *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed. Cir. 2005) (en banc). Moreover, ‘the person of ordinary skill in the art is deemed to read the claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the

specification.” *ICU Med., Inc. v. Alaris Med. Sys.*, 558 F.3d 1368, 1374 (Fed. Cir. 2009). Thus, one of ordinary skill in the art would interpret a compound of formula (I) or its salts “or a protected form thereof” *after having read the entire specification*, including the information set forth on Page 5, Lines 22-25, and would readily understand what is meant. That meaning is reinforced by the representative number of suitable protection groups that are explicitly set forth in the specification. *See, e.g., Specification, Page 5, Line 22 to Page 6, Line 4.*

It is also important to recognize that “a patent claim is not necessarily invalid for lack of written description just because it is broader than the specific examples disclosed.” *Martek Biosciences Corp. v. Nutrinova, Inc.*, 579 F.3d 1363, 1371 (Fed. Cir. 2009) (citing *Bilstad v. Wakalopulos*, 386 F.3d 1116, 1123 (Fed. Cir. 2004)). Indeed, “in the context of written description, the fact ‘that a claim may be broader than the specific embodiment disclosed in a specification is in itself of no moment.” *Martek*, 579 F.3d at 1371 (citing *In re Rasmussen*, 650 F.2d 1212, 1215 (C.C.P.A. 1981)). While the Examiner argues that the disclosed species are not representative of the genus, a “specification may, within the meaning of 35 U.S.C. § 112, para. 1, contain a written description of a broadly claimed invention without describing all species that the claim encompasses.” *Cordis Corp. v. Medtronic AVE, Inc.*, 339 F.3d 1352, 1365 (Fed. Cir. 2003) (quoting *Utter v. Hiraga*, 845 F.2d 993, 998 (Fed. Cir. 1988)).

Moreover, by the present amendment Applicants amended independent Claim 49 to specify that “a protected form thereof” is one wherein one or more of the hydroxyl groups at positions 4, 5, and/or 6 are protected by a protection group. This amendment

was made solely to facilitate prosecution and not to acquiesce to the Examiner's rejection.

Because one of ordinary skill in the art would appreciate that Applicants were in possession of the subject matter of Claims 49-51 and 70-82 at the time of filing, Applicants respectfully request withdrawal of the written description rejection of Claims 49-51 and 70-82.

Rejections Under 35 U.S.C. § 112, Second Paragraph – Indefiniteness

Claims 49-51 and 70-82 were rejected under 35 U.S.C. § 112, Second Paragraph, as purportedly indefinite due to the phrase "2'-deoxynucleoside precursors." See *Office Action mailed January 25, 2010, Pages 8-9*. These rejections are respectfully traversed.

"Definiteness of claim language must be analyzed, not in a vacuum, but in light of: (A) The content of the particular application disclosure; (B) The teachings of the prior art; and (C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made." *Manual of Patent Examining Procedure ("M.P.E.P.") § 2173.02*.

Applicants submit that the meaning of "2'-deoxynucleoside precursors" is readily apparent to one of ordinary skill in the art at least due to the information contained at Page 5, Lines 9-16, of the specification. While the Examiner asserts that the metes and bounds of the claimed methods are not readily apparent, Applicants respectfully disagree. "Breadth of a claim is not to be equated with indefiniteness. *In re Miller*, 441 F.2d 689, 169 USPQ 597 (CCPA 1971)." *M.P.E.P. § 2173.04*. Again, at least Page 5,

Lines 9-16, of the specification set forth for one of ordinary skill in the art

“2'-deoxynucleoside precursors.” “If the scope of the subject matter embraced by the claims is clear, and if applicants have not otherwise indicated that they intend the invention to be of a scope different from that defined in the claims, then the claims comply with 35 U.S.C. 112, second paragraph.” *M.P.E.P.* § 2173.04.

Moreover, by the present amendment Applicants amended independent Claim 49 to specify that the “2'-deoxynucleoside precursors” are 2-deoxy-D-ribose (DRI) or carbohydrate compounds which can be converted into the 2-deoxy-D-ribosyl moiety of 2'-deoxynucleosides, including 1-phospho-2-deoxy-D-ribose, 5-phospho-2-deoxy-D-ribose, 2-deoxy-D-ribitol, 2-deoxy-D-ribonic acid, 2-deoxy-D-ribono-1,4-lactone, 1-N-morpholino-3,4,5-trihydroxy-pentene-1, and their derivatives. This amendment was made solely to facilitate prosecution and not to acquiesce to the Examiner's rejection.

Because one of ordinary skill in the art would readily appreciate what is meant by “2'-deoxynucleoside precursors,” Applicants respectfully request withdrawal of the rejection of Claims 49-51 and 70-82 under 35 U.S.C. § 112, Second Paragraph.

Rejections Under 35 U.S.C. § 102 – Wong

Claims 49-51, 70-74,² 78, and 81 were rejected under 35 U.S.C. § 102(b) as purportedly anticipated by U.S. Patent No. 5,759,825 to Wong (“Wong”). *See Office Action mailed January 25, 2010, Pages 9-13.* These rejections are respectfully traversed.

² Applicants believe the Examiner did not intend to reject Claims 68 and 69, as those claims were canceled in Applicants' Amendment and Reply filed on October 8, 2009.

"Invalidity based on 'anticipation' requires that the invention is not in fact new." *Verve LLC v. Crane Cams, Inc.*, 311 F.3d 1116, 1120 (Fed. Cir. 2002). To be anticipating, a "single reference must describe the claimed invention with sufficient precision and detail to establish that the subject matter existed in the prior art." *Verve*, 311 F.3d at 1120. "To anticipate, every element and limitation of the claimed invention must be found in a single prior art reference, arranged as in the claim." *Brown v. 3M*, 265 F.3d 1349, 1351 (Fed. Cir. 2001).

Applicants respectfully submit that each and every element of Claims 49-51, 70-74, 78, and 81 are not found in Wong. The Examiner admits that "Wong is silent as to the decarboxylation reaction effected by pyruvate decarboxylase." *Office Action mailed January 25, 2010, Page 11*. Yet, the Examiner asserts "it is reasonable to believe that the enzyme pyruvate decarboxylase in the mixture disclosed by Wong would inherently act upon said aldol disclosed by Wong according to the method of the instant invention." *Office Action mailed January 25, 2010, Page 12*. The mere possibility or even probability that the mixture of Wong would behave as the Examiner suggest is not legally sufficient to establish anticipation. "Anticipation by inherent disclosure is appropriate only when the reference discloses prior art that must *necessarily* include the instated limitation." *Therasense, Inc. v. Becton, Dickinson & Co.*, 593 F.3d 1325, 1332 (Fed. Cir. 2010). "Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing *may* result from a given set of circumstances is not sufficient." *Therasense*, 593 F.3d at 1332 (quoting *Continental Can Co. USA, Inc. v. Monsanto Co.*, 948 F.2d 1264, 1269 (Fed. Cir. 1991)). Instead, "[i]nherent anticipation requires that the missing descriptive material is 'necessarily

present,' not merely probably or possibly present, in the prior art." *Therasense*, 593 F.3d at 1332 (quoting *Trintec Indus., Inc. v. Top-U.S.A. Corp.*, 295 F.3d 1292, 1295 (Fed. Cir. 2002)).

Because Wong does not *necessarily* contain each and every element of Claims 49-51, 70-74, 78, and 81, Applicants respectfully request withdrawal of the 35 U.S.C. § 102(b) rejection thereof.

Rejections Under 35 U.S.C. § 103 – Wong and Candy

Claims 49-51, 70-78,³ and 81 were rejected under 35 U.S.C. § 103(a) as purportedly obvious over Wong in view of J. M. Candy *et al.*, "*Structure and properties of pyruvate decarboxylase and site-directed mutagenesis of the Zymomonas mobilis enzyme*," 1385 BIOCHIMICA ET BIOPHYSICA ACTA 323-338 (1998) ("Candy"). See *Office Action mailed January 25, 2010, Pages 13-16*. These rejections are respectfully traversed.

"A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. § 103(a). Underlying factual determinations in an obviousness analysis include (1) the scope and content of the prior art, (2) the level of ordinary skill in the art, (3) the differences

³ Applicants believe the Examiner did not intend to reject Claims 68 and 69, as those claims were canceled in Applicants' Amendment and Reply filed on October 8, 2009.

between the claimed invention and the prior art, and (4) objective indicia of nonobviousness. *Merck & Co. v. Teva Pharms. USA, Inc.*, 395 F.3d 1364, 1369 (Fed. Cir. 2005) (citing *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966)).

Applicants respectfully submit that a *prima facie* case of obviousness against Claims 49-51, 70-78, and 81 due to Wong in view of Candy has not been made.

It is important to recognize that each of Claims 49-51, 70-78, and 81 must be considered *as a whole*. See, e.g., *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1742 (2007) ("What matters is the objective reach of the claim."); *Datascope Corp. v. SMEC, Inc.*, 776 F.2d 320, 324 (Fed. Cir. 1985) (noting that the references must be considered "as a whole" and that the claimed subject matter must be considered "as a whole."). Considering each of Claims 49-51, 70-78, and 81 as a whole is important because "a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *KSR*, 127 S. Ct. at 1741. That is because "inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." *Id.*

The Examiner admits that "Wong is silent as to the decarboxylation reaction effected by pyruvate decarboxylase." *Office Action mailed January 25, 2010, Page 11*. The Examiner also admits that Wong does not disclose pyruvate decarboxylases of prokaryotic origin, as required by Claims 75-77. *Office Action mailed January 25, 2010, Page 14*. Applicants respectfully submit that only by using impermissible hindsight would one modify Wong and Candy as the Examiner suggests to arrive at Applicants' Claims 49-51, 70-78, and 81. Yet, factfinders must avoid the distortion caused by

hindsight bias “and must be cautious of arguments reliant upon *ex post* reasoning.”

KSR, 127 S. Ct. at 1742 (citing *Graham* and “warning against a ‘temptation to read into the prior art the teachings of the invention in issue’ and instructing courts to ‘guard against slipping into the use of hindsight.’”).

In addition to the arguments presented by Applicants in their Amendment and Reply filed on October 8, 2009, Applicants stress that the methods of Claims 49-51, 70-78, and 81 rely upon a substrate compound of formula (I) having 6 carbon atoms, wherein there is an acid function on carbon atom 1, a ketone function on carbon atom 2, and no function on carbon atom 3. Contrarily, Wong “is directed to an enhanced process for synthesizing 2-ketoaldonic acids.” *Wong*, Column 2, Lines 6-7. Wong defines 2-ketoaldonic acids as: $\text{CH}_2\text{OH}-(\text{CHOH})_{n-1}-\text{CO}-\text{COOH}$. *Wong*, Column 1, Lines 33-35. Wong arrives at such 2-ketoaldonic acids by mixing an aldolase with an excess of pyruvate and an acceptor substrate aldose. See, e.g., *Wong*, Column 2, Lines 5-34 and the Claims. Put differently, Applicants’ claimed methods produce 2’-deoxynucleosides or 2’-deoxynucleoside precursors using a compound of formula (I) that undergoes a single-step enzymatic decarboxylation; whereas Wong mixes an aldolase, an excess of pyruvate, and an acceptor substrate aldose in an aqueous solvent so that “condensation of the pyruvate with the acceptor substrate aldose [forms] a ketoaldonic acid.” Compare Claims 49-51, 70-78, and 81 with *Wong*, Column 2, Lines 6-22.

Accordingly, Applicants respectfully request withdrawal of the rejection of Claims 49-51, 70-78, and 81 under 35 U.S.C. § 103(a) over Wong in view of Candy.

Rejections Under 35 U.S.C. § 103 – Wong and CRC

Claims 49-51, 70-74,⁴ 81, and 82 were rejected under 35 U.S.C. § 103(a) as purportedly obvious over Wong in view of the CRC Handbook of Chemistry and Physics (“the CRC”). See *Office Action mailed January 25, 2010, Pages 16-18*. These rejections are respectfully traversed.

The deficiencies of Wong are detailed above. Applicants submit that the CRC does not cure these deficiencies. Again, Wong neither discloses nor suggests Applicants’ claimed methods. Applicants’ claimed methods produce 2'-deoxynucleosides or 2'-deoxynucleoside precursors using a compound of formula (I) that undergoes a single-step enzymatic decarboxylation. Wong does not employ such methods. Instead, Wong mixes an aldolase with an excess of pyruvate and an acceptor substrate aldose in an aqueous solvent so that “condensation of the pyruvate with the acceptor substrate aldose [forms] a ketoaldonic acid.”

Accordingly, Applicants respectfully request withdrawal of the rejection of Claims 49-51, 70-74, 81, and 82 under 35 U.S.C. § 103(a) over Wong in view of the CRC.

⁴ Applicants believe the Examiner did not intend to reject Claims 68 and 69, as those claims were canceled in Applicants’ Amendment and Reply filed on October 8, 2009.

CONCLUSION

In the event that there are any questions relating to this Supplemental Reply To Final Office Action Pursuant To 37 C.F.R. § 1.116 And Statement Of The Substance Of The Interview, or to the application in general, it would be appreciated if the Examiner would contact the undersigned attorney by telephone at (703) 836-6620 so that prosecution of the application may be expedited.

The Patent Office is hereby authorized to charge any necessary fees, or credit any overpayment, to Deposit Account No. 02-4800.

Respectfully submitted,
BUCHANAN INGERSOLL & ROONEY PC

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